Table S1 GO term analyses of genetic modifiers of *His1* effect on viability.

Gene Symbol	Biological evidence for the gene and/or gene product	Reference(s)
Chromosome organization (biological function), GO:0051276		
nopo	Fly homolog of human E3 ligase TRIP; interacts with DNA polymerase η, regulates S to M transition during syncytial nuclear divisions.	(Wallace et al. 2014) (Merkle et al. 2009)
AGO1	Component of miRNA-specific silencing machinery; was shown to regulate nuclear organization of PcG target loci.	(Williams and Rubin 2002) (Grimaud et al. 2006)
CG3358	Fly ortholog of TatD-related DNAse TATDN1 that plays an important role in mitotic chromosome segregation.	(Yang et al. 2012)
Sep5	Nuclear GTPase and a component of microtubule-associated complex involved in cytokinesis.	(Hughes et al. 2008) (Goldstein and Gunawardena 2000)
E(Pc)	Contributes to chromatin-dependent silencing; is not present in PRC1 or PRC2 but, rather, is a subunit of histone acetyltranferase complex TIP60 involved in both gene activation and repression; interacts with *ISWI*, which is involved in H1 deposition into chromatin.	(Sinclair et al. 1998) (Stankunas et al. 1998) (Kusch et al. 2004) (Arancio et al. 2010)
Elba2	BEN domain-containing protein; associates with the *Fab-7* boundary/insulator element, promotes chromatin silencing.	(Aoki et al. 2012)
Socs36E	SH2 domain-containing suppressor of cytokine signaling; a negative regulator of the JAK/STAT cascade, which is involved, together with H1, in the establishment of heterochromatin silencing.	(Singh et al. 2010) (Xu et al. 2014)
c(2)M	Component of the synaptonemal complex; required for reciprocal meiotic recombination.	(Heidmann et al. 2004)
Chd1	ATP-dependent nucleosome remodeling motor protein; essential for chromatin assembly in the nascent male pronucleus and for deposition of H3.3 at transcriptionally active loci.	(Konev et al. 2007)
DNA binding (molecular function), GO:0003677		
bsh	Brain-specific homeobox protein.	(Hasegawa et al. 2013)
vis	Homeobox-containing TGIF-related transactivator.	(Hyman et al. 2003)
inv	Helix-turn-helix transcription factor.	(Simmonds et al. 1995)
zf30C	Zinc finger transcription factor.	(Jafari et al. 2012)
CG3358	Fly ortholog of TatD-related DNAse TATDN1.	(Yang et al. 2012)
CG12744	Zinc finger transcription factor.	(Jin et al. 2008)
lola	Zinc finger transcription factor.	(Giniger et al. 1994)
Elba2	BEN domain-containing protein, associates with the *Fab-7* element.	(Aoki et al. 2012)
Chd1	ATP-dependent nucleosome remodeling motor protein.	(Konev et al. 2007)
c(2)M	Component of the synaptonemal complex.	(Heidmann et al. 2004)
Small GTPase-mediated signal transduction (biological function), GO:0007264		
phyl	Regulator of Notch and Wnt signaling pathways.	(Nagaraj and Banerjee 2009)
CG15611	Exhibits sequence similarity to fly Rho guanyl-nucleotide exchange factor TRIO.	(Bateman et al. 2000)
CG8155	Structurally similar to fly Rab GTPase activator Evi5.	(Laflamme et al. 2012)
GEFmeso	Mesoderm guanine nucleotide exchange, a binding target of Ras-like GTPase Ral.	(Blanke and Jackle 2006)
RtGEF	Homologous to mammalian Rho-type guanyl-nucleotide exchange factor Pix.	(Manser et al. 1998)
Arf51F	GTP-binding protein according to sequence similarity to human ADP-ribosylation factor 2, Arf2.	(Bobak et al. 1989)
Sep5	Belongs to the superfamily of Septin GTPases.	(O'Neill and Clark 2013)
Gametogenesis (biological function), GO:0048477, GO:0007283		
gbb	Fly ortholog of human bone morphogenic protein-5 (BMP-5); was shown to be involved in BMP signaling that controls ovarian cell development.	(Kirilly et al. 2005)
vis	Transcription factor; required for regulation of multiple genes involved in sperm manufacture; mutants are male sterile due to a defect in primary	(Ayyar et al. 2003)

	spermatocyte differentiation before the onset of meiotic divisions.	
TBCB	Tubulin-binding cofactor B, a ubiquitin-related domain-containing protein; regulates microtubule organization in the nucleus and controls oocyte polarity.	(Baffet et al. 2012)
AGO1	Plays central roles in female germ-line cell differentiation.	(Yang et al. 2007)
Arf51F	ADP ribosylation factor; is required for cytokinesis in spermatocytes.	(Dyer et al. 2007)
stau	dsRNA- and mRNA 3'-UTR-binding protein; regulates translation and mRNA localization of egg polarity genes *bicoid*, *gurken*, *nanos* and *oskar*.	(Johnstone and Lasko 2001)
Lar	Leukocyte antigen-related-like tyrosine phosphatase receptor protein; required for the establishment of cell polarity during oogenesis.	(Krueger et al. 2003)
Edtp	Egg-derived tyrosine phosphatase; essential for ovarian development, oogenesis and embryogenesis.	(Yamaguchi et al. 2005)
Socs36E	Functions in male germ-line stem cell maintenance.	(Issigonis et al. 2009) (Singh et al. 2010)
pAbp	Polyadenylate-binding protein; essential for spermatid elongation; translationally regulates Grk (*gurken*), which is required for the establishment of the dorsal-ventral axis of a developing egg.	(Pertceva et al. 2010) (Clouse et al. 2008)
Chd1	SNF2-like ATPase; functions in oogenesis and egg fertilization.	(Konev et al. 2007) (McDaniel et al. 2008)
Nervous system development and neural system processes (biological function), GO:0007399, GO:0050877		
Dap160	Dynamin-associated protein, contains EF-hand and SH3 domains, a negative regulator of Notch signaling; interacts with the atypical protein kinase C (aPKC) to stimulate neuroblast proliferation; similar to dynamin, regulates synaptic vesicle endocytosis.	(Chabu and Doe 2008) (Koh et al. 2004)
bsh	Transcription factor; regulates neuronal identity specification.	(Hasegawa et al. 2013)
phyl	Zinc-binding protein; essential for the peripheral nervous system development and photoreceptor differentiation.	(Chang et al. 1995)
gbb	Part of the BMP signaling pathway; important for the neuromuscular junction development and synaptic transmission.	(James and Broihier 2011)
CG5742	Predicted ankyrin repeat-containing protein; was found to regulate neurogenesis in an RNAi screen in vivo in *Drosophila*.	(Neumuller et al. 2011)
inv	Transcription factor; regulates neuroblast fate determination.	(Bhat and Schedl 1997)
lea	Axon guidance receptor; regulates neuron migration.	(Simpson et al. 2000) (Kraut and Zinn 2004)
zf30C	Transcription factor; regulates dendrite morphology in the developing brain.	(Parrish et al. 2006)
spict	Magnesium transmembrane transporter orthologous to human NIPA1; negatively regulates BMP signaling to promote synaptic growth at the neuromuscular junction.	(Wang et al. 2007)
Pka-R2	cAMP-dependent protein kinase R2; functions in repulsive axon guidance.	(Terman and Kolodkin 2004)
spi	TGF-α-like ligand that triggers epidermal growth factor receptor (EGFR) activation to promote neuroepithelial proliferation and neuroblast formation in the optic lobe; as a component of EGFR signaling pathway, is important for olfactory learning in flies.	(Morante et al. 2013) (Rahn et al. 2013)
RtGEF	Rho-type guanine nucleotide exchange factor; regulates postsynaptic structure and protein localization at the glutaminergic neuromuscular junction.	(Parnas et al. 2001)
uzip	Cell adhesion protein; functions in axon guidance in the *Drosophila* central nervous system.	(Ding et al. 2011)
Arf51F	GTP-binding protein; has a regulatory function in synaptic vesicle endocytosis.	(Lloyd et al. 2000)
stau	Regulator of translation, a major player in the establishment of long-term memory and neuronal plasticity.	(Dubnau et al. 2003)
lola	Transcription factor; regulates axonogenesis, brain morphogenesis and eye development.	(Giniger et al. 1994) (Yamamoto et al. 2008) (Zheng and Carthew 2008)

Lar	Tyrosine phosphatase receptor; plays a key role in the control of axon guidance.	(Krueger et al. 1996)
E(Pc)	Together with other subunits of the TIP60 HAT complex regulates dendrite targeting of olfactory neurons.	(Tea and Luo 2011)
Stress response (biological function), GO:0006955, GO:0006952		
nopo	E3 ligase; likely plays a role in defense response, based on its homology with human TRAF-interacting protein TRIP.	(Lee et al. 1997)
coro	WD40 repeat-containing protein; belongs to a family of proteins involved in defense response to fungus.	(Jin et al. 2008)
Gbp	Growth blocking peptide; a potent cytokine that stimulates the expression of anti-microbial peptides.	(Tsuzuki et al. 2012)
lola	Transcription factor; functions in anti-microbial humoral response.	(Kleino et al. 2005)
CG13551	ATPase inhibitor, glycine-rich protein; has an in vitro activity in suppressing Gramm-positive bacteria.	(Feng et al. 2009)
dnr1	FERM domain- and RING finger-containing protein; an inhibitor of the immune deficiency (IMD) pathway at the level of initiator caspase Dredd.	(Guntermann et al. 2009)
Jhl-21	Leucine transmembrane transporter; belongs to a family of proteins involved in defense response to fungus.	(Jin et al. 2008)
Traf4	TNF receptor-associated factor; functions in the IMD pathway and plays a role in fly defense response to *Vibrio cholera*.	(Berkey et al. 2009)

The known attributes and properties of genetic suppressors and enhancers of *His1* function in vivo that belong to enriched GO term classes are listed.